

**REMARKS**

Claims 1 and 3-11 constitute the pending claims in this application. Claim 2 has been canceled without prejudice. The subject matter of claim 2 has been included in independent claim 1. Claim 1 has been amended for greater clarity. The claim amendments are supported by the specification (e.g., on page 12, lines 8-12 and 14-17). No new matter has been introduced. The amendments are made solely to expedite prosecution of the application, and Applicants reserve the right to prosecute claims of similar or differing scope in subsequent applications.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

**Claim rejections under 35 U.S.C. § 102**

Claims 1-3 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Hotz et al. (Mol. Biochem. Parasitology, 75:1-14, 1995). Claims 1-3 are also rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Treco et al. (US Patent No. 6,063,630). Applicants traverse these rejections to the extent it is maintained over the claims as amended.

The standard for anticipating a claim is clearly outlined in MPEP 2131, and this standard is further supported by the Courts. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1978). "The identical invention must be shown in as complete detail as is contained in the claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Applicants contend that Hotz et al. and Treco et al. each fails to satisfy this criteria for anticipating the present invention. As amended, independent claim 1 relates to a method for removing the 3'-untranslated region of a population of DNA molecules, wherein each DNA molecule in said population of DNA molecules comprises an open reading frame and a 3'-untranslated region, said method comprising: (a) providing a population of DNA molecules, each of said DNA molecules terminating at its 5' end in a 3' DNA chain overhang and at its 3'

end in a blunt end; and (b) treating each of said DNA molecules first with an exonuclease III and then with a single-stranded nuclease under conditions that allow removal of said 3'-untranslated region, wherein the sequential treatment of said DNA molecules with the exonuclease III and the nuclease specifically removes the 3'-untranslated region from the 3' end.

Hotz et al. provide a working example where DNA molecules amplified by using primers containing ApaI and XhoI sites were digested with exonuclease and mung bean nuclease (page 2, col. 2, paragraph 2.1; page 3, col. 1, lines 1-13). Contrary to the Examiner's assertion, Hotz et al. fail to teach that DNA molecules terminate at its 5' end in a 3' DNA chain overhang and at its 3' end in a blunt end after digestion with ApaI and XhoI. Also, contrary to the Examiner's assertion, Hotz et al. fail to teach that exonuclease III and mung bean nuclease were added sequentially (with exonuclease III being used first and mung bean nuclease being used later). Further, Hotz et al. do not teach or suggest that use of exonuclease III and the nuclease specifically removes the 3'-untranslated region from the 3' end. Accordingly, the teachings of Hotz et al. do not meet the limitations of the instant claims.

Treco et al. describe a method of converting the ends of HindIII digested DNA molecules from a double-stranded form to a single-stranded form using exonuclease III. Treco et al. also describe that mung bean nuclease was added to exonuclease treated DNA in order to monitor the extent of digestion and the length of the 5'-overhangs. See, col. 17, lines 8-45. Contrary to the Examiner's assertion, Treco et al. do not teach that HindIII digested DNA molecules terminate at its 5' end in a 3' DNA chain overhang and at its 3' end in a blunt end. In fact, one of skill in the art would readily know that HindIII digested DNA molecules terminate at both 5' and 3' ends in 5' overhangs and thus cannot meet this limitation of the instant claims. Further, Treco et al. do not teach specific removal of the 3'-untranslated region from the 3' end by nuclease treatment. Because the HindIII digested DNA molecules have the same 5' overhangs at both ends (5' and 3'), one of skill in the art would know that treatment of exonuclease III would delete sequences from both ends (5' and 3'). Indeed, Treco et al. describe that "ExoIII digestion of the HindIII digested DNA results in extensive exonucleolytic digestion at each end ..." (emphasis added) (col. 17, lines 18-19). Accordingly, the teachings of Treco et al. do not meet the limitations of the instant claims.

In view of the above, Applicants respectfully submit that Hotz et al. and Treco et al. fail

to meet the limitations of the present claims and thus fail to anticipate the claimed subject matter. Reconsideration and withdrawal of this rejection are respectfully requested.

Claim rejections under 35 U.S.C. § 103(a)

Claims 4-11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hotz et al. in view of Szostak et al. (US Patent No. 6,214,553). Applicants traverse these rejections to the extent it is maintained over the claims as amended.

Pursuant to MPEP 2143, “[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the reference themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.”

As discussed above, Hotz et al. fail to anticipate the subject matter as recited in amended independent claim 1. Specifically, Hotz et al. do not teach 1) the feature of the 5’ end (in a 3’ overhang) and the 3’ end (in a blunt end) of the DNA molecule, 2) sequential treatment with an exonuclease III and a single stranded nuclease, and 3) specific removal from the 3’ end of the 3’-untranslated region. Applicants submit that Szostak et al. cited by the Examiner fail to bridge the gap between Hotz et al. and the claimed invention.

In addition, a skilled artisan would not have had a reasonable expectation of success even if, for the sake of argument, the Hotz reference were combined with the Szostak reference. As a matter of fact, one of skill in the art would recognize that Hotz’ method would result in removal of DNA sequences from the 5’ end because the XhoI digestion generates a 5’-overhang at the 5’ end, thereby creating a substrate sequence for exonuclease III to act from the 5’ end (see a printout on Exonuclease III from New England Biolabs, enclosed herewith as **Exhibit A**). Thus, Hotz et al. teach away from the present invention which recites specific removal from the 3’ end, not the 5’ end, of the DNA molecule.

In view of the remarks and claim amendments set forth above, Applicants submit that independent claim 1 is patentably non-obvious over Hotz. In addition, Applicants submit that all

claims depending from claim 1 recite further limitations thereon, and hence are a fortiori patentably non-obvious over Hotz. Reconsideration and withdrawal of rejection under 35 U.S.C. § 103(a) is respectfully requested.


**CONCLUSION**

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the claims are now in condition for allowance and early notification to this effect is earnestly solicited. Any questions arising from this submission may be directed to the undersigned at (617) 951-7000.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. COTH-P03-504 from which the undersigned is authorized to draw.

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Respectfully submitted,

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